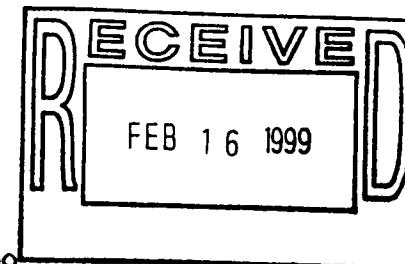


# WINE INSTITUTE

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JOHN A. DE LUCA  
PRESIDENT

February 12, 1999

Dr. C.W. Jameson  
NTP Report on Carcinogens  
MD EC-14  
P.O. Box 12233  
Research Triangle Park, NC 27709

**RE: Alcohol and the Ninth Report on Carcinogens**

Dear Dr. Jameson:

Wine Institute, the public policy association of 450 California wineries, respectfully takes this opportunity to communicate further public comments regarding the Review Committees' vote on listing consumption of alcoholic beverages in the Report on Carcinogens. We formally request a deferment of a final decision until Committee members have had adequate time to review all the relevant literature and, if appropriate, propose more careful wording that reflects current science fairly and precisely.

In reviewing the remarks from the NTP Committee meeting regarding "alcoholic beverage consumption" on December 2, 1998, it is clear that many concerns about listing alcoholic beverages as a known human carcinogen were not yet addressed or discussed adequately. The state of confusion reflected in the transcript reveals a scientific debate to which there is not yet clarity—and is not nearly ready for a final vote. Based on the Committee meeting transcript, we urge you to address the following issues:

- **A more complete review of literature:** A more careful Committee review of peer-reviewed literature is necessary, with clear guidelines concerning what is included in the review and what is omitted. Studies that clearly distinguish between moderate alcohol intake and heavy intake should be more closely examined.
- **Alcohol independent of tobacco:** Evidence of alcohol consumption's role in cancer incidence must be found without cigarette smoking confounding. Alcohol's role should be established independent of other factors, and if that cannot be done adequately, wording should reflect it.
- **Other issues affecting wording:** The Committee members did not have adequate time to discuss possible additions or qualifications to the wording, although many suggestions were made. Favorable health effects at moderate levels, synergistic effects with confounders, dose distinctions, "alcoholic lifestyles," other components in beverages and other issues mentioned must be adequately discussed and considered.

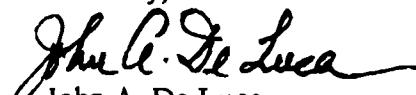
- **Voting process confusion:** There needs to be a clearer process for the discussion, proposed wording changes and voting for Committee members.

As the peer-reviewed literature will attest, the issue of moderate versus heavy consumption and its relation to cancer is far from resolved. As dozens of epidemiological and biochemical studies show, the health effects of moderate consumption are very different from those of excessive consumption. In a recent study published in the Archives of Internal Medicine (Camargo et al., 1997, See attached table), Harvard researchers conclude, "The difference between consumption of small and large amounts of alcohol may mean the difference between preventing and causing excess mortality." To ignore this distinction reflects an oversight too important for a public document like the NTP Report on Carcinogens. We do not believe it is unwarranted for the NTP Committee to reconsider this point and allow for changes in wording, as the importance of moderate health effects was brought up, but not pursued, in the meeting.

The extensive scientific evidence in the attached table demonstrates that moderate alcohol consumption has been independently associated with lower overall mortality rates in dozens of studies. Listing "consumption of alcoholic beverages" as a known human carcinogen, based almost entirely on evidence at heavy intake levels, does not serve the public health of the country—or the overwhelming majority of American who consume wine, beer and spirits moderately.

Given the exceptional importance of the matter before you, we urge you to defer a final determination until all issues are adequately addressed. It would be historically unjustified for the NTP to rush to judgment before it was able to more accurately reflect current scientific knowledge.

Sincerely,



John A. De Luca  
President & CEO

JDL:kc  
Attachments

## ALCOHOL, WINE AND OVERALL MORTALITY – KEY STUDIES 1998-1990

Muntyler J, Gaziano JM, et al.

**Mortality and light to moderate alcohol consumption after myocardial infarction.**

*Lancet*, 1998; 352:1882-1885.

Drawing from a pool of over 90,000 men from the Harvard University Physicians' Health Study, researchers found that for men with a previous heart attack "moderate alcohol intake was associated with a significant decrease in total mortality." Those drinking two to six drinks a week at the lowest risk for dying compared to nondrinkers. Drinkers had reduced risks for both cardiovascular and non-cardiovascular mortality, and younger men between ages 40 and 64 had the same protection as old ones. The researchers conclude, "Our results show that men with a history of myocardial infarction with a light to moderate intake of alcohol have a slight but clinically important decrease in total mortality, compared to those who never or rarely drink alcohol."

Maskarinec, et al.  
**Alcohol intake, body weight, and mortality in a multiethnic prospective cohort.**  
*Epidemiology*, 1998; 9:654-661.

Analyzing data from a prospective, multicohort study of more than 40,000 people in Hawaii, researchers found light to moderate drinkers to have an overall lower risk for dying compared to abstainers. "In agreement with previous reports," they write, "this study found that persons with moderate alcohol intake appear to have a lower risk of dying than nondrinkers, but the possible protective levels of alcohol for women and Asian men appear to be lower than for Caucasian men." After adjustment for other factors, men overall who consumed from one to 28 drinks per week had a reduced risk for all-cause mortality of 14-22 percent. For women overall, all-cause mortality rates were reduced by 18 percent for consumers of 1-7 drinks per week, with a slight reduction for consumption levels a bit higher. The researchers explain, "A 20% reduction in overall mortality for individuals with low alcohol intake as compared with abstainers is consistent with findings shown in several publications."

Renard SC, et al.  
**Alcohol and mortality in middle-aged men from Eastern France.**  
*Epidemiology*, 1998; 9(1):184-188.

This study of a cohort of 34,000 middle-aged French men found a significant reduction in all-cause mortality, cardiovascular disease and all types of cancers among those who consumed alcohol, mostly wine, moderately. Moderate consumption of approximately to 2-3 glasses of wine a day was associated with a 30 percent reduction in the death rate from all causes; a 35 percent reduction in the death rate from cardiovascular disease; and an 18-24 percent reduction in death rates from all cancer. The authors conclude, "The results of the present prospective study, the first in France on the health effects of moderate wine drinking, appear to confirm the speculation that the so-called 'French paradox' is due, at least in part, to the regular consumption of wine."

Deev A, Irving S, et al.  
**Association of alcohol consumption to mortality in middle-aged U.S. and Russian men and women.**  
*Annals of Epidemiology*, 1998; 8(3):147-153.

The authors assessed the relationship of alcohol consumption to total mortality in U.S. and Russian men, aged 40-59, and women, aged 40-69. They found that "lower level" drinkers in both genders and countries had lower age-adjusted mortality rates than nondrinkers. When adjusting mortality rates for other risk factors, only U.S. men and women had clear mortality advantages. They conclude that for U.S. men and women "mortality rates are significantly lower for drinkers than non-drinkers after adjustment for several variables," but "beneficial effects of alcohol consumption on mortality may be limited depending upon other mortality risk factors populations under study."

**Investigation****Background/Summary of Findings**

Doll R.  
**One for the heart.**  
*BMJ*, 1997; 315:1664-1668.

Citing "massive" evidence for the beneficial effect of alcohol, a leading British researcher provides a clinical review of alcohol and mortality. Based on data from three dozen studies published over the past decade, he concludes that the consumption of small and moderate amounts of alcohol leads to a one-third risk reduction for vascular disease and a reduction in total mortality. Addressing the public health implications of such findings, he writes, "People should be treated as adults and should be told the facts. These still need to be refined in detail, but in broad outline they are quite clear: in middle and old age some small amount of alcohol in the range of one to four drinks each day reduces the risk of premature death, irrespective of the medium in which it is taken."

Thun MJ, et al.  
**Alcohol consumption and mortality among middle-aged and elderly adults.**  
*The New England Journal of Medicine*, 1997; 337(24):1705-1714.

In the largest study on alcohol consumption to date, researchers analyzing data from nearly 500,000 people in the Cancer Prevention Study II reported that overall death rates for those who drink moderately were lower compared to those who did not drink at all. While risks to liver cirrhosis and certain cancers were found to increase with alcohol intake, researchers state, "The overall death rates were lowest among men and women reporting about one drink daily," with a reduced all-cause mortality risk of approximately 20 percent. Rates of death from all cardiovascular diseases combined were 30 to 40 percent lower among men and women reporting at least one drink daily than among nondrinkers.

Yuan J-M, et al.  
**Follow up study of moderate alcohol intake and mortality among middle aged men in Shanghai China.**  
*BMJ*, 1997; 314:18-23.

In the first large-scale study on moderate alcohol use in a Chinese population, researchers analyzed data from over 18,000 middle-aged Chinese men who drank alcohol moderately. They found that "regular drinkers of alcohol had a 19% lower death rate than non-drinkers" and "Death rates among moderate drinkers were lower for cancer and non-cancer causes." With heart disease accounting for only 9 percent of deaths in this population, other mortality risks including chronic bronchitis, cirrhosis, injuries and certain cancers were notable in their reduced associations for moderate drinkers.

Canarigo CA, et al.  
**Prospective study of moderate alcohol consumption and mortality in US male physicians.**  
*Archives of Internal Medicine*, 1997; 157:79-85.

Analyzing data from the Physicians' Health Study, a prospective cohort study of 22,071 men, Harvard University researchers found a more favorable mortality profile for light and moderate drinkers compared to nondrinkers. Compared to men who consumed less than one drink per week, the risk of deaths from all causes was 28% lower for a man who had 2 to 4 drinks per week, and 21% lower for one who had 5 to 6 drinks per week. In relation to cancer, the researchers state, "Our results provide strong support for the conclusions of previous epidemiological studies of both fatal and nonfatal cancer, which found little (if any) increased cancer risk among men who were light to moderate drinkers." They conclude, "The difference between consumption of small and large amounts of alcohol may mean the difference between preventing and causing excess mortality." The highest category of consumption, "2 or more drinks per day," had the most unfavorable mortality profile, although the researchers acknowledge that this open-ended category fails to distinguish between daily moderate drinkers and alcohol abusers.

Simons LA, et al.  
**Examining the relationship between all-cause mortality and alcohol intake from 1236 men and 1569 women**

**Investigation study****Health outcome summary of 1 studies**

**Alcohol intake and survival in the elderly: a 77 month follow-up in the Dubbo study.**  
*Australian and New Zealand Journal of Medicine*, 1996; 26:662-670.

followed for 77 months, Australian researchers found that "alcohol intake appears to confer a survival advantage," with an inverse relationship for men and "potentially a U-shaped relationship" for women. For categories of one to seven drinks/week, eight-14 drinks/week and 15-28 drinks/week, men had reduced risks for all-causes mortality of 25%, 24% and 31%, and women had reduced risks of 22%, 51% and 38%, respectively. They conclude, "Alcohol intake in the Dubbo elderly appears to be independently associated with a significant increase in life expectancy."

Holman CDJ, et al.

**Meta-analysis of alcohol and all-cause mortality: A validation of NHMRC recommendations.**  
*Medical Journal of Australia*, 1996; 164(3):141-145.

Evaluating the National Health and Medical Research Council (NHMRC) recommendations on responsible levels of alcohol intake—up to 28 units per week for men and up to 14 units per week for women—this review examined the relative risks of mortality in relation to usual level of alcohol intake in 16 cohort studies, and alcohol intake and selected conditions from a further 132 epidemiological studies. Compared with abstainers, one to two daily drinks for men and up to one drink for women reduced all-cause mortality by approximately 12 to 16 percent. While some cancer risks increased, all-cause mortality risk was reduced for men drinking up to three drinks per day and women up to two drinks per day. The researchers conclude, "A pattern of usual alcohol intake consistent with NHMRC recommendations will confer a mortality risk similar to or less than that observed in abstainers."

Gronbaek M, et al.

**Mortality associated with moderate intakes of wine, beer, or spirits.**  
*BMJ*, 1995; 310: 1165-1169.

The Copenhagen City Heart Study examined the association between intake of different types of alcohol beverages and mortality in 6051 men and 7234 women aged 30-70 years at 10-12 years follow-up between 1976 and 1988. The results showed the risk of dying steadily decreased with an increasing intake of wine, reducing chance of death from cardiovascular and cerebrovascular disease by over 50 percent, as well as other causes of death by 20 to 50 percent, at one to five drinks per day compared to abstention. The researchers write, "The wine drinkers experienced a significantly lower all cause mortality than the subjects who drank no wine," noting that consumption of beer or spirits was not clearly associated with reduced risk. They conclude, "Low to moderate intake of wine is associated with lower mortality from cardiovascular and cerebrovascular disease and other causes," and suggest that the potential protective effects of phenolic compounds in wine may play a role in these results.

Fuchs CS, et al.

**Alcohol consumption and mortality among women.**  
*The New England Journal of Medicine*, 1995; 332(19):1245-1250.

Analyzing data from the ongoing Nurses' Health Study of 85,709 women, 34 to 59 years of age, Harvard researchers found the relative risks of death in drinkers as compared with nondrinkers were reduced by 17 percent for women who consumed 1.5 to 4.9 g of alcohol per day (one to three drinks per week), reduced by 12 percent at 5.0 to 14.9 g per day, reduced by 11 percent at 15 to 29.9 g per day and increased by 19 percent for those who consumed 30 g or more per day. They write, "As compared with nondrinkers and heavy drinkers, light-to-moderate drinkers had a significantly lower overall risk of death." They note that the mortality benefits were most apparent for those at risk for coronary heart disease and those over the age of 50. The largest of its kind to find mortality benefits for light-to-moderate drinking for women, the study also found no increase in breast cancer risk at one drink per day and a nonsignificant overall trend towards more protection from wine.

**Investigation/Study**      **Findings/Summary of findings**

<p>Duffy JC.</p> <p><b>Alcohol consumption and all-cause mortality.</b></p> <p><i>International Journal of Epidemiology</i>, 1995; 24: 100-105.</p>	<p>This review by a Scottish researcher, analyzing a number of studies using logistic-linear modeling, found abstention from alcohol to be a special risk factor for mortality, though not sufficient to fully explain the observed protective effect. He analyzes two British studies in depth, noting that the current accepted sensible consumption level in the U.K. "may be slightly less than the optimal level." He concludes, "Hence on this analysis, alcohol consumption, rather than being a cause of premature mortality, is a net preventer of such."</p>	<p>Cannelli D, Christian JC, et al.</p> <p><b>World War II-veteran male twins who are discordant for alcohol consumption: 24-year mortality.</b></p> <p><i>American Journal of Public Health</i>, 1995; 85(1):99-101.</p>	<p>Using the National Academy of Sciences/National Research Council World War II-Veteran Twin Male Registry, this study investigated the role of genetic and shared environmental influences in the association of alcohol with mortality. Analyzing groups of twins who had discordant alcohol consumption patterns for 24 years, the researchers found more deaths in abstainer group than the light-to-moderate drinking group. Excess mortality in twin abstainers was indicated for deaths from cardiovascular diseases and other causes of death excluding cancers, with smoking minimizing any protective effects of alcohol. The researchers state, "In the present study, monozygotic abstainers had an excess of death from all causes compared with their light-to-moderate-drinking cotwins."</p>	<p>Doll R, Peto R, et al.</p> <p><b>Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors.</b></p> <p><i>BMJ</i>, 1994; 309: 911-918.</p>	<p>Drawing from a pool of British men in middle or older age over a period of 13 years, this study found that the consumption of alcohol appeared to reduce the risk of ischaemic heart disease, largely irrespective of amount, and that there were significantly fewer deaths in moderate drinkers than in nondrinkers. Those reporting eight to 14 drinks per week appeared to have the lowest risks for death, with those consuming over 21 units progressively increasing their chances of death. The researchers conclude, "Among British men in middle or older age the consumption of an average of one or two units of alcohol a day is associated with significantly lower all-cause mortality than is the consumption of no alcohol, or the consumption of substantial amounts."</p>	<p>Coate D.</p> <p><b>Moderate drinking and coronary heart disease mortality: evidence from NHANES I and NHANES I follow-up.</b></p> <p><i>American Journal of Public Health</i>, 1993; 83(6): 888-890.</p>	<p>Data from the National Health and Nutrition Examination Survey (NHANES I), conducted from 1971 through 1974, and the NHANES I Follow-up, conducted from 1982 through 1984, were used to test for an effect of moderate alcohol consumption on coronary heart disease mortality among white men and women. While no "important effect" was shown for women, "accelerated time-to-failure models showed for men a 3% to 4% longer life span for moderate drinkers than for nondrinkers or light drinkers." The researcher concludes, "These results are consistent with a substantial body of previous research that finds a protective effect of moderate drinking on coronary heart disease mortality for White men."</p>
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Investigation / study		
Cullen KJ, et al.  Alcohol and mortality in Busselton, Western Australia.  <i>American Journal of Epidemiology</i> , 1993; 137(2):242-248.	The authors analyzed 23-year mortality in 2,171 subjects at least 40 years of age from a Busselton, Western Australia, prospective study. The analysis revealed significant inverse associations between alcohol consumption and mortality, with trends of decreasing mortality shown from nondrinkers to mild drinkers to moderate drinkers. Compared with nondrinkers, moderate drinkers had a reduced risk of death due to all causes of 24 percent, and a reduction of over 30 percent for cardiovascular disease. The researchers write, "In conclusion, results from this 23-year study support the hypothesis that mild to moderate alcohol drinking reduces the risk of premature death."	This study, examining responses from 1,823 male subjects in a twelve-year follow-up time period, found incidence rates of overall mortality to be the lowest for moderate drinkers in each of three age groups. Testing hypotheses that other factors of ill health may explain a protective effect, the researchers separate out former drinkers in their analyses and still find "lifetime teetotalers had two to five times the risk for overall and CHD mortality compared to those who described themselves as occasional, regular or former drinkers." They conclude, "These results lend support to the hypothesis of the beneficial effect of moderate drinking, with respect to mortality."
De Labry LO, et al.  Alcohol consumption and mortality in an American male population: recovering the U-shape curve: findings from the normative aging study.  <i>Journal of Studies on Alcohol</i> 1992; 53(1): 25-32.	Farchi G, et al.  Alcohol and mortality in the Italian rural cohorts of the Seven Countries Study.  <i>International Journal of Epidemiology</i> . 1992, 21(1):74-82.	The relation of alcohol consumption to mortality was examined using prospective data from 1536 men aged 45-64 of the Italian rural cohorts of the Seven Countries Study. According to the researchers, "The analysis shows a J-shaped relationship between alcohol consumption, expressed as a percentage of total daily energy intake, and both overall mortality and cardiovascular mortality; this J-shaped relationship is evident even after adjusting for age, cigarette smoking and occupation." The low and moderate consumption categories were associated with reduced risks for all causes of death, and the researchers note that this population of middle-aged Italian men drank almost exclusively wine, usually at mealtimes.
Klatsky AL, et al.  Alcohol and mortality.  <i>Annals of Internal Medicine</i> , 1992; 117: 646-644.	Using data from over 128,000 adults, researchers summarize the risks of heavy drinking and report that the relative risk for death is decreased for both men and women who have approximately one drink per day. The greatest reduction is found in older persons, while women and younger persons appear more susceptible to the increased mortality risk of heavy drinking. The researchers also note that wine preference was associated with a significantly lower relative risk for cardiovascular death. They write, "For the sexes combined, the lower risk [of death] of lighter drinkers was significant," with the lower risk "substantially, but not entirely, due to deaths from cardiovascular causes."	5

**Investigation/Study****Background/Summary of findings**

Boffetta P and Garfinkel L.  
**Alcohol drinking and mortality among men enrolled in an American Cancer Society Prospective Study.**  
*Epidemiology*, 1990; 1(5):342-348.

Analyzing data from a large American Cancer Society study of over 276,000 men, the researchers found relative risks of total mortality to be reduced 12 percent for occasional drinkers, 16 percent for those having one drink per day, and seven percent for those having two drinks per day. For occasional drinkers or those who drink one drink per day, a slight reduction in cancer mortality was also suggested. The researchers refute the hypothesis that the U-shaped relation between alcohol and mortality is caused by the inclusion of diseased nondrinkers and write, "Our results on moderate drinkers are consistent with those found in several populations for both total and CHD mortality."

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